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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER
KIM, YOUNG J

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	09/816,763	REMACLE ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8,12-22,34,36,37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,12-19,21,22,34,36,37,39 and 40* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 1, 2007 has been entered.

Priority

The Office acknowledges the receipt of the certified copy of the foreign document to which Applicants claim foreign priority as required by 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

The IDS received on May 1, 2007 is acknowledged.

The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Applicants' particular attention is directed to reference #3, where the name of the inventor, "Wu et al." is erroneous. In addition, the U.S. Patent No. 5,846,683 is titled, "Toner producing methods using recycled extra-fine toner particles," which appears to have nothing to do with the instant invention.

Claim Objections

The objection of claims 19 and 21 made in the Office Action mailed on November 14, 2006 is withdrawn in view of a careful consideration.

The objection of claim 20 made in the Office Action mailed on November 14, 2006 is maintained for the reasons already of record, however.

It is maintained that claim 20 is drawn to an invention that is distinct from claim 1, for the following reasons.

Claim 1, to which the above claims depend from, is drawn to a method which comprises the step of binding transcriptional factors to immobilized double-stranded DNAs.

Claim 20 is drawn to a method for screening, quantifying and/or recovering ***compounds*** which modulate the activity of enzymes or proteins acting on transcriptional factors which are then further assay for their binding to the transcriptional factors.

Hence, claim 20 is not assaying for the activated transcriptional factors, but rather, assaying for compounds which modulates the activity of enzymes, proteins.

Claim 20 has not been further treated on its merits.

While Applicants contend that the claims had been amended to become drawn to a method of the elected invention, it is respectfully submitted that claim 20 is drawn to a method of screening for modulators of enzymes and proteins.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8, 12, 15, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 are indefinite for reciting an intended use for the method of claim 1, but failing to recite the active steps required to achieve the intended use.

While minor details are not required in method/process claims, at least the basic steps must be recited in a positive, active fashion. See *Ex parte Elrich*, 3 USPQ2d, p. 1011 (Bd. Pat App. Int. 1986).

Claim 12 recites the limitation, "the insoluble solid support."

There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites the phrase, "wherein the double-stranded DNA sequences fixed on the support surface contain in part or totally one or several of the specific DNA sequences presented in the table 1. The term, "totally" confers that the support must have all of the attributes (i.e, the specific DNA sequences presented in the table 1. However, the claim recites that support contains totally one or several, which contradicts the meaning of the term, "totally."

Claim 21 recites the phrase, "step of identifying transcriptional factors..." However, its parent claim 1 recites that the identification step is for active transcriptional factors. Hence, it becomes unclear whether the subject-phrase is referring to the active transcriptional factors or another set of transcriptional factors.

In addition, the phrase, "peptides which are part of the transcriptional factor(s) active complex," render the phrase unclear in ascertaining whether the transcriptional factor(s) active complex" ***is*** the active transcriptional factor(s) employed in parent claim 1.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 2, 4-8, 12-18, 22, 36, and 37 under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, issued October 8, 1996) in view of

Heslot et al. (U.S. Patent No. 6,342,353 B1, issued January 29, 2002, 102(e) date November 4, 1999) and Nerenberg et al. (US 2002/0015198 A1, published August 22, 2002, filed September 20, 2001, priority September 20, 2000), made in the Office Action mailed on November 14, 2006 is withdrawn in view of the Amendment received on May 1, 2007.

The rejection of claim 34 under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, issued October 8, 1996) in view of Heslot et al. (U.S. Patent No. 6,342,353 B1, issued January 29, 2002, 102(e) date November 4, 1999) and Nerenberg et al. (US 2002/0015198 A1, published August 22, 2002, filed September 20, 2001, priority September 20, 2000) as applied to claims 1, 2, 6-8, 12-18, 22, 36, and 37 above, and further in view of Dattagupta et al. (U.S. Patent No. 4,968,602, issued November 6, 1990), made in the Office Action mailed on November 14, 2006 is withdrawn in view of the Amendment received on May 1, 2007.

Rejection, New Grounds

Claims 1, 2, 4-8, 12-19, 21, 22, 36, 37, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, issued October 8, 1996) in view of Brand et al. (Journal of Clinical Investigation, 1996, vol. 97, pages 1715-1722), Heslot et al. (U.S. Patent No. 6,342,353 B1, issued January 29, 2002, 102(e) date November 4, 1999) and Nerenberg et al. (US 2002/0015198 A1, published August 22, 2002, filed September 20, 2001, priority September 20, 2000).

Peterson et al. disclose a method comprising the steps of: a) binding to a solid substrate (thus insoluble), such as microtiter plate (column 5, line 34-36; column 7, line 23; column 8, lines 59-60), double-stranded DNA sequences (column 6, lines 26-28), at the concentration greater than 0.01 pmoles/cm^2 (column 10, line 26), wherein said double-stranded DNA is connected to the surface of

the solid support via avidin-biotin binding (column 7, lines 13-18) or antigen/antibody binding (column 7, lines 18-19); b) contacting transcriptional factors with said solid-surface bound double-stranded DNAs (column 3, lines 1-5; column 4, lines 37-41); and c) identifying and/or quantifying a signal resulting from the binding of the transcriptional factors to said solid-surface bound double-stranded DNAs (column 8, lines 64-68).

Peterson et al. do not explicitly teach that their method should be directed to assaying/screening/quantifying for activated transcriptional factors.

Peterson et al. do not teach that the double-stranded DNAs is connected to the surface of the solid-surface support by *a spacer* comprising at least a *double-stranded* DNA nucleotide sequence of between about 50 and about 250 base pairs.

Peterson et al. do not explicitly teach that the solid-support be an array bearing at least 4 spots/cm^2 of solid support surface.

Peterson et al., while explicitly disclosing that their method involves transcriptional factors that may be derived from, "a host or from ***an infectious or parasitic organisms***" (column 3, lines 9-13), as well as HIV TAT (Table 1, column 5, lines 21-25), do not explicitly disclose that the transcriptional factor be HIV Integrase.

Brand et al. evidences the art-recognized importance of identifying activated form of transcriptional factors, such as NF-kB (Abstract).

Heslot et al. disclose a method involving the immobilization of double-stranded DNA (column 1, lines 9-10) via a spacer arm which is also double-stranded DNA (column 4, lines 36-37), wherein said spacer arm comprises the length of 5 to 1kb in length (column 4, lines 39-40), for the explicit purpose of providing "freedom of movement." (column 4, lines 16-17).

Nerenberg et al. disclose a well-known use of sensor array comprising high-density array of immobilized nucleic acids, wherein artisans ***explicitly*** disclose that the sensor array of the invention would be useful in screening in "a solution analytes that might be transcriptional factors such as activators or repressors." [0134]. Nerenberg et al. also explicitly disclose that nucleic acid binding to integrase is measured in their sensor [0134].

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Peterson et al. with those of Brand et al., Heslot et al. and Nerenberg et al. to arrive at the invention as claimed for the following reasons.

Initially, the use of spacer arms in an array technology for the purpose of providing freedom to immobilized ligands have been known and established in the art. Previously cited Saiki et al. document as well as the disclosure of Heslot et al. supports such knowledge.

Therefore, one of ordinary skill in the art at the time the invention was made would have been easily motivated to modify the teachings of Peterson et al. with the use of any spacer arm for the advantage of providing freedom to immobilized ligands. One of ordinary skill in the art at the time the invention was made also would have had a clear expectation of success at using a double-stranded DNA spacer arm in conjunction with the method of Peterson et al. because Heslot et al. explicitly demonstrated that such combination would work, as well as disclosing that either double-stranded or other known polymers would work as effectively (column 4, lines 40-45).

MPEP, at 2143.02 states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success. As already discussed above, one of ordinary skill in the art would have had a clear expectation of success at using a double-stranded DNA spacer arm in combination with the method disclosed by Peterson et al. as the use of such technologies has been well-known, enabled, and established in the art.

In addition, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the method of Peterson et al., for the purpose of screening/quantifying for activated transcriptional factors for the following reasons.

Brand et al. evidences the importance of activated transcriptional factors, such as NF-kB, wherein the artisans state:

> "Several lines of evidence indicate that NF-kB/Rel transcription factors play an important role in atherosclerosis...A variety of genes are induced in the atherosclerotic lesion that have been shown to be regulated by NF-kB proteins, including the genes encoding TNF-α...IL-1β...macrophage colony-stimulating factor (M-CSF)...GM-CSF...monocyte chemotactic protein-1...tissue factor (TF)...vascular cell adhesion molecule-1...intercellular adhesion molecule-1 (ICAM-1)...and c-myc." (page 1715, 2nd column, 2nd paragraph).

In detecting the activated form of the NF-kB transcriptional factors, Brand et al., however, employ Electrophoretic Mobility Shift Assay (EMSA) (see page 1716, 2nd column, 2nd paragraph).

Given the fact that Peterson et al. explicitly state that their invention allows for the high-throughput screening of analyzing transcriptional factors binding in response to candidate drugs (column 2, lines 53-55), one of ordinary skill in the art at the time the invention was made would have been clearly motivated to screen for activated transcriptional factors, which are implicated with known physiological conditions, so as to diagnose, and screen for possible candidate drugs which may interfere with the activity of said activated transcriptional factors.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success at combining the teachings since Brand et al. provides for the teaching of labeling only the activated form of NF-kB transcriptional factors, that is, by use of an antibody which is specific for p65 subunit of NF-kB, wherein p65 subunit is masked by an IkB in an inactivated form.

Since Peterson et al.'s method also labels the protein (column 6, lines 7-8) prior to their binding with DNA sequences, one of ordinary skill in the art would have been able to label the activated transcriptional factors based on the teachings of Brand et al., followed by their binding to the DNA sequences of Peterson et al., with a clear expectation of success.

With regard to the density limitation of the solid support being an array comprising at least 4 spots per cm^2, the advantage of using a high-density microarray has been well-established in the art as allowing multiple reactions in a miniaturized area, and whether the surface comprise at least 4 spots or any number of spots would be well-within the purview of an ordinarily skilled artisan in the art of array technology.

Therefore, for the above reasons, claims 1, 6, 8, 12-19, 21, 22, 36, 37, 39, and 40 are obvious over the cited references.

With regard to claim 2, Peterson et al. disclose the transcriptional factor being present at a concentration lower than 20 nM (column 10, lines 40-41).

With regard to the labeling being non-radioactive (instant claim 4) or obtained through enzymatic reactions (instant claim 5), Peterson et al. disclose that the labeling could be luminescence (or non-radioactive), or indirect detection such as epitope tag, an enzyme (column 6, lines 13-17).

With regard to the transcription factors being selected from those recited in the Markush group of claim 7, Peterson et al. disclose a plurality of the recited transcriptional factors in their Table 1 (beginning at column 3, line 30 through column 5).

With regard to screening for compounds that modulate the binding of transcriptional factors (instant claim 18), Peterson et al. disclose that the mixture applied as a sample comprises candidate pharmacological compounds that comprise functional chemical groups necessary for structural interactions with proteins and/or DNA (column 5, line 35; column 7, lines 28-46).

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, issued October 8, 1996) in view of Brand et al. (Journal of Clinical Investigation, 1996, vol. 97, pages 1715-1722), Heslot et al. (U.S. Patent No. 6,342,353 B1, issued January 29, 2002, 102(e) date November 4, 1999) and Nerenberg et al. (US 2002/0015198 A1, published August 22, 2002, filed September 20, 2001, priority September 20, 2000), as applied to claims 1, 2, 4-8, 12-19, 21, 22, 36, 37, 39, and 40 above, and further in view of Dattagupta et al. (U.S. Patent No. 4,968,602, issued November 6, 1990).

The teachings of Peterson et al., Brand et al., Heslot et al., and Nerenberg et al. have been already discussed above.

While Peterson et al. explicitly disclose that avidin/biotin binding could be employed for immobilizing double-stranded DNA, none of the artisans explicitly disclose that streptavidin, in place of avidin could be employed.

Dattagupta et al. explicitly state that biotin can be coupled to either ***avidin or streptavidin*** (column 18, lines 32-37).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the avidin with streptavidin of Dattagupta et al. to arrive at the claimed method involving streptavidin/biotin binding for the following reaons.

MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as ***prima facie*** obvious as long as there is a reasonable expectation of success. Given that the use of avidin or streptavidin for its binding with biotin for the purpose of immobilizing nucleic acids have

been well-established in the art as established by the date of the patent of Dattagupta et al. as well as their explicit teaching, one of ordinary skill in the art at the time the invention was made would have had a clear expectation of success at modifying the teachings of Peterson et al., Brand et al., Heslot et al., and Nerenberg et al. to arrive at the invention as claimed.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Double Patenting - Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 1, 2, 4-8, 12-18, 22, 34, 36, and 37 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21, 25, and 26 of copending Application No. 10/821,568, made in the Office Action November 14, 2006 is maintained for the reasons already of record.

In addition, claims 39 and 40 are rejected herein as being necessitated by amendment (their addition).

The Rejection:

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

Independent claim 1 of the instant application and claim 1 of the '568 application are both drawn to a method of detection involving solid-support bound double-stranded DNA and transcriptional factors, wherein said solid-support bound double-stranded DNA are immobilized to the solid support via a spacer of certain length. Claim 1 of the '568 application recites that said spacer comprises a length of about 6.8 nm, while claim 1 of the instant application recites that the length is from about 50 to 250 base pairs, both ranges of which would necessarily overlap.

While the method of signal generation involved in the '568 application is drawn to antibody, the instant invention embraces such detection method as embraced by the generic detection method recited in claim 1 – non radioactive signal.

The transcriptional factors involved in the method of the instant claims and claims of the '568 application are selected from the same Table 1 (see instant claim 7, claim 16 of the '568 application).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments:

Applicants' request to hold the rejection in abeyance until allowable subject matter is identified is noted.

At the present state, the claims are not in condition for allowance, and accordingly, the rejection is maintained for the reasons of record.

Conclusion

No claims are allowed.

Applicant's arguments with respect to previous rejections of record have been considered but are moot in view of the new ground(s) of rejection.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
7/10/2007

YOUNG J. KIM
PRIMARY EXAMINER

YJK